Human neural stem cells improve cognition and promote synaptic growth in two complementary transgenic models of Alzheimer's disease and neuronal loss.

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Public Summary:

Scientific Abstract:
Alzheimer's disease (AD) is the most prevalent age-related neurodegenerative disorder, affecting over 35 million people worldwide. Pathologically, AD is characterized by the progressive accumulation of ss-amyloid (Ass) plaques and neurofibrillary tangles within the brain. Together, these pathologies lead to marked neuronal and synaptic loss and corresponding impairments in cognition. Current treatments, and recent clinical trials, have failed to modify the clinical course of AD; thus, the development of novel and innovative therapies is urgently needed. Over the last decade, the potential use of stem cells to treat cognitive impairment has received growing attention. Specifically, neural stem cell transplantation as a treatment for AD offers a novel approach with tremendous therapeutic potential. We previously reported that intrahippocampal transplantation of murine neural stem cells (mNSCs) can enhance synaptogenesis and improve cognition in 3xTg-AD mice and the CaM/Tet-DTA model of hippocampal neuronal loss. These promising findings prompted us to examine a human neural stem cell population, HuCNS-SC, which has already been clinically tested for other neurodegenerative disorders. Here, we provide the first evidence that transplantation of research grade HuCNS-SCs can improve cognition in two complementary models of neurodegeneration. We also demonstrate that HuCNS-SC cells can migrate and differentiate into immature neurons and glia, and significantly increase synaptic and growth-associated markers in both 3xTg-AD and CaM/Tet-DTA mice. Interestingly, improvements in aged 3xTg-AD mice were not associated with altered Ass or tau pathology. Rather, our findings suggest that human NSC transplantation improves cognition by enhancing endogenous synaptogenesis. Taken together, our data provide the first preclinical evidence that human NSC transplantation could be a safe and effective therapeutic approach for treating AD.